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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,896	07/14/2003	Paul G. Ahlquist	960296.00096	7353

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

NOTIFICATION DATE	DELIVERY MODE
10/15/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

Office Action Summary	Application No.	Applicant(s)	
	10/618,896	AHLQUIST ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-30* is/are pending in the application.

4a) Of the above claim(s) *21-25 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-14-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of group IV, claims 26 and 27, in the reply filed on 8-28-07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 21-25 and 28-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8-28-07.

Applicants' preliminary amendment filed on 7-14-03 has been entered. Claims 1-20 have been canceled. Claims 21-30 are pending. Claims 26 and 27 are under consideration.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "a method of evaluating a substance as an antiviral therapy" in line 1 of claims 26 and 27 is vague and renders the claims indefinite. Am "antiviral therapy" appears to be a method or a type of therapy. It is unclear how a "substance" can be an "antiviral therapy".

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 26 and 27 read on using a delta9 fatty acid desaturase enzyme derived from various organisms, such as humans, rats, mice, canine, feline, sheep, cows, horses, monkeys, whales, other mammals, insects, birds, fish etc. The specification only discusses delta9 fatty acid desaturase enzyme encoded by OLE1 gene in yeast. A search of OLE1 gene in the art only results in the OLE1 gene of Histoplasma capsulatum (a dimorphic pathogenic fungus) and OLE1 gene of yeast Saccharomyces cerevisiae at the time of the invention, i.e. 6-12-97.

The claims encompass a genus of numerous different delta9 fatty acid desaturase enzymes derived from various organisms, such as humans, rats, mice, canine, feline, sheep, cows, horses, monkeys, whales, other mammals, insects, birds, fish etc., and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification fails to provide the structural features that contribute to the biological function of various delta9 fatty acid desaturase enzymes. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the

disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the discussion of the yeast OLE1 gene or enzyme in the present application is insufficient to describe the genus.

Therefore, the limited information provided in the present invention is not sufficient to reasonably convey to one skilled in the art that applicants were in possession of the genus of numerous different delta9 fatty acid desaturase enzymes derived from various organisms. Thus, it is concluded that the written description requirement is not satisfied for the use of the genus of numerous different delta9 fatty acid desaturase enzymes derived from various organisms as claimed.

7. Claims 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considered whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirement, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of

ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d at 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

Furthermore, the USPTO does not have laboratory facilities to test if an invention with function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raises and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

Claims 26 and 27 are drawn to a method of evaluating a substance as an antiviral therapy comprising exposing a substance to a delta9 fatty acid desaturase enzyme and evaluating the effect of the substance on the enzyme, wherein decrease in stability or inhibition of activity indicates that the substance is a possible antiviral therapy.

The specification discloses that brome mosaic virus (BMV) is a positive-strand RNA virus and the use of yeast Saccharomyces cerevisiae for virus replication studies (p. 2, 2nd paragraph). Ole1 protein is the desaturase that converts SFAs to UFAs (p. 49, lines 1-2). "BMV RNA replication did not require the Ole1 protein but rather required UFA levels well above those required for cell growth" (p. 47, 1st paragraph). "BMV RNA replication is strongly dependent on UFA levels in vivo. When UFA was limited, ER-associated RNA replication was blocked after 1a and 2a membrane association and RNA3 template recognition and stabilization, but before negative-strand RNA synthesis. The ability to use ole1w mutation to block RNA replication at this stage should help to elucidate the early events in initiating RNA synthesis.

Dependence of BMV RNA replication on UFA levels in particular implies a requirement for host membrane fluidity" (p. 51, 2nd paragraph).

The claims encompass using various delta9 fatty acid desaturases (OLE1 proteins) for evaluating a substance as an antiviral therapy by exposing a substance to the OLE1 proteins, wherein decrease in stability or inhibition of activity indicates that the substance is a possible antiviral therapy.

As discussed above under 35 U.S.C. 112 first paragraph, written description requirement, the claims encompass a genus of numerous different delta9 fatty acid desaturase enzymes derived from various organisms, such as humans, rats, mice, canine, feline, sheep, cows, horses, monkeys, whales, other mammals, insects, birds, fish etc., and the specification fails to provide the structural features that contribute to the biological function of various delta9 fatty acid desaturase enzymes (OLE1 proteins). Applicants do NOT have possession of the claimed various OLE1 proteins. Absent such possession, one skilled in the art would not know how to use the various OLE1 proteins to practice the claimed invention, and would require undue experimentation to practice over the full scope of the invention claimed.

The specification fails to provide adequate guidance and evidence for the whether decrease in stability or inhibition of activity of various OLE1 proteins would be indicative of potential antiviral therapy. The specification fails to provide a correlation between decrease in stability or inhibition of activity of various OLE1 proteins and the antiviral therapy. The specification shows that although Ole1w yeast mutant inhibits BMV-directed gene expression (p. 31, line 14-16), however, "BMV RNA replication did not require the Ole1 protein but rather required UFA levels well above those required for cell growth" and "BMV RNA replication is

strongly dependent on UFA levels in vivo... Dependence of BMV RNA replication on UFA levels in particular implies a requirement for host membrane fluidity" (p. 51, 2nd paragraph). It appears that UFA level is a more important factor than OLE1 protein in blocking BMV RNA replication. There is no evidence of record that shows a correlation between a decrease in stability or inhibition of activity of various OLE1 proteins and an antiviral therapy. There is no evidence of record that a substance effecting a decrease in stability or inhibition of activity of various OLE1 proteins would be indicative of said substance as an antiviral therapy agent.

Even if there is a correlation between a decrease in stability or inhibition of activity of various OLE1 proteins and an antiviral therapy, different OLE1 proteins could have different biological functions and there is no evidence of record that shows those different OLE1 proteins would have same effect on the BMV RNA replication or various viral infections. Since OLE1 proteins other than the yeast OLE1 protein might not have any effect on BMV RNA replication or any viral infection. Therefore, a substance effecting a decrease in stability or inhibition of activity of those OLE1 proteins would not be indicative of said substance as an antiviral therapy agent.

It was known in the art that the amino acid sequence of a polypeptide determines its structural and functional properties (including half-life), and predictability of which amino acid(s) can be removed from or added to a polypeptide's sequence and still result in similar activity or result in stabilization of the protein is extremely complex, and well outside the realm of routine experimentation. Rudinger, 1976 (Peptide Hormones, Parsons, University Park Press, Baltimore, p. 1-7) points out that "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from

case to case by painstaking experimental study" (e.g. p. 6). Kaye et al., 1990 (Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 6922-6926) discloses that a single amino acid substitution results in a retinoblastoma protein defective in phosphorylation and oncoprotein binding (e.g. title). In addition, Skolnick et al., 2000 (Trends in Biotech, Vol. 18, p. 34-39) states "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for prediction of multiple functional sites. Structural descriptors for protein functional sites are crucial for unlocking the secrets in both the sequence and structural-genomics projects" (e.g. abstract). Skolnick further states that "Knowing a protein's structure does not necessarily tell you its function" and "Because proteins can have similar folds but different functions, determining the structure of a protein may or may not tell you something about its function" (e.g. p. 36, box 2). Therefore, biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention. The biological functions of various OLE1 proteins were unpredictable at the time of the invention. The specification fails to disclose structural feature or functional domain that contributes to the biological function of the yeast (Saccharomyces cerevisiae) OLE1 protein and fails to provide adequate guidance and evidence for whether those OLE1 proteins would have the same biological function as the yeast OLE1 protein. Absent such guidance, one skilled in the art at the time of the invention would not know whether a substance effecting a decrease in stability or inhibition of activity of those OLE1 proteins would be indicative of said substance as an antiviral therapy agent.

Further, there are numerous type of viruses, for example, single strand (positive and negative) and double strand RNA viruses, and single and double strand DNA viruses, and viral

infection caused by those different viruses vary morphologically, physiologically and pathologically. The mechanisms of viral infection and the strategy of antiviral therapy for different viral infections would vary depending on the type of viral infection. Thus, a substance identified via its effect in decreasing stability or inhibiting activity of OLE1 protein maybe a possible antiviral agent for a particular viral infection but said substance would not necessarily be a possible antiviral agent for various other viral infections.

For the reasons set forth above, one skilled in the art at the time of the invention would have to engage in undue experimentation to practice over the full scope of the invention claimed. This is particularly true based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, the level of skill which is high, the amount of experimentation required, and the breadth of the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER